

CLAIMS

What is claimed is:

1. An isolated polypeptide comprising a functional SLC26A6 polypeptide.
- 5 2. The functional SLC26A6 polypeptide of claim 1 comprising:
 - (a) a polypeptide encoded by a nucleic acid of any one of odd-numbered SEQ ID NOs:1-7;
 - (b) a polypeptide encoded by a nucleic acid substantially identical to any one of odd-numbered SEQ ID NOs:1-7;
 - 10 (c) a polypeptide comprising an amino acid sequence of any one of even-numbered SEQ ID NOs:2-8; or
 - (d) a polypeptide substantially identical to any one of even-numbered SEQ ID NOs:2-8.
3. The functional SLC26A6 polypeptide of claim 1, wherein the
15 SLC26A6 polypeptide is encoded by an isolated nucleic acid segment selected from the group consisting of:
 - (a) an isolated nucleic acid molecule encoding a polypeptide of any one of even-numbered SEQ ID NOs:2-8;
 - (b) an isolated nucleic acid molecule of any one of odd-numbered
20 SEQ ID NOs:1-7;
 - (c) an isolated nucleic acid molecule which hybridizes to a nucleic acid sequence of any one of odd-numbered SEQ ID NOs:1-7 under wash stringency conditions represented by a wash solution having less than about 200 mM salt concentration and
25 a wash temperature of greater than about 45°C, and which encodes a functional SLC26A6 polypeptide; and
 - (d) an isolated nucleic acid molecule differing by at least one functionally equivalent codon from the isolated nucleic acid molecule of one of (a), (b), and (c) above in nucleic acid
30 sequence due to the degeneracy of the genetic code, and which encodes a functional SLC26A6 polypeptide encoded by the isolated nucleic acid of one of (a), (b), and (c) above.

4. The functional SLC26A6 polypeptide of claim 1, wherein the functional property comprises Cl^- -formate exchange.
5. The functional SLC26A6 polypeptide of claim 1, wherein the functional property comprises Cl^- - Cl^- exchange.
- 5 6. The functional SLC26A6 polypeptide of claim 1, wherein the functional property comprises SO_4^{2-} exchange.
7. The functional SLC26A6 polypeptide of claim 1, wherein the functional property comprises Cl^- -oxalate exchange.
8. The functional SLC26A6 polypeptide of claim 8, wherein the
10 functional property comprises Cl^- -base exchange.
9. The functional SLC26A6 polypeptide of claim 8, wherein the base comprises HCO_3^- .
10. The functional SLC26A6 polypeptide of claim 1, wherein the Cl^- -base exchange comprises electrogenic transport.
- 15 11. A system for recombinant expression of a functional SLC26A6 polypeptide, the system comprising:
 - (a) a functional SLC26A6 polypeptide; and
 - (b) a host cell comprising the functional SLC26A6 polypeptide.
12. The system of claim 11, wherein the host cell comprises a
20 mammalian cell.
13. The system of claim 12, wherein the mammalian cell comprises a human cell.
14. An isolated nucleic acid encoding a human SLC26A6a polypeptide.
15. The isolated nucleic acid of claim 14, further comprising a nucleic acid
25 encoding a polypeptide of SEQ ID NO:2.
16. The isolated nucleic acid of claim 14, further comprising a nucleic acid of SEQ ID NO:1.
17. An isolated human SLC26A6a polypeptide.
18. The isolated human SLC26A6a polypeptide of claim 17, further
30 comprising:
 - (a) a polypeptide of SEQ ID NO:2; or
 - (b) a polypeptide encoded by a nucleic acid molecule of SEQ ID NO:1.

19. A system for recombinant expression of a human SLC26A6a polypeptide, the system comprising:
- (a) a human SLC26A6a polypeptide; and
 - (b) a host cell comprising the human SLC26A6a polypeptide.
- 5 20. An isolated nucleic acid encoding a mouse SLC26A6 polypeptide.
21. The isolated nucleic acid of claim 20, further comprising a nucleic acid encoding a polypeptide of SEQ ID NO:6 or 8.
22. The isolated nucleic acid of claim 20, further comprising a nucleic acid of SEQ ID NO:5 or 7.
- 10 23. An isolated mouse SLC26A6 polypeptide.
24. The isolated mouse SLC26A6 polypeptide of claim 23, further comprising:
- (a) a polypeptide of SEQ ID NO:6 or 8; or
 - (b) a polypeptide encoded by a nucleic acid molecule of SEQ ID
- 15 NO:5 or 7.
25. A system for recombinant expression of a mouse SLC26A6 polypeptide, the system comprising:
- (a) a mouse SLC26A6 polypeptide; and
 - (b) a host cell comprising the mouse SLC26A6 polypeptide.
- 20 26. A method for identifying a modulator of a SLC26A6 polypeptide, the method comprising:
- (a) providing a recombinant expression system whereby a functional SLC26A6 polypeptide is expressed in a host cell;
 - (b) providing a test substance to the system of (a);
 - 25 (c) assaying a level or quality of SLC26A6 function in the presence of the test substance;
 - (d) comparing the level or quality of SLC26A6 function in the presence of the test substance with a control level or quality of SLC26A6 function; and
 - 30 (e) identifying a test substance as an anion transport modulator by determining a level or quality of SLC26A6 function in the presence of the test substance as significantly changed when compared to a control level or quality of SLC26A6 function.

27. The method of claim 26, wherein the functional SLC26A6 polypeptide comprises:

- (a) a polypeptide encoded by a nucleic acid of any one of odd-numbered SEQ ID NOs:1-7;
- 5 (b) a polypeptide encoded by a nucleic acid substantially identical to any one of odd-numbered SEQ ID NOs:1-7;
- (c) a polypeptide comprising an amino acid sequence of any one of even-numbered SEQ ID NOs:2-8; or
- 10 (d) a polypeptide substantially identical to any one of even-numbered SEQ ID NOs:2-8.

28. The method of claim 26, wherein the functional SLC26A6 polypeptide is encoded by an isolated nucleic acid segment selected from the group consisting of:

- 15 (a) an isolated nucleic acid molecule encoding a polypeptide of any one of even-numbered SEQ ID NOs:2-8;
- (b) an isolated nucleic acid molecule of any one of odd-numbered SEQ ID NOs:1-7;
- (c) an isolated nucleic acid molecule which hybridizes to a nucleic acid sequence of any one odd-numbered SEQ ID NOs:1-7
- 20 under wash stringency conditions represented by a wash solution having less than about 200 mM salt concentration and a wash temperature of greater than about 45°C, and which encodes a functional SLC26A6 polypeptide; and
- (c) an isolated nucleic acid molecule differing by at least one
- 25 functionally equivalent codon from the isolated nucleic acid molecule of one of (a), (b), and (c) above in nucleic acid sequence due to the degeneracy of the genetic code, and which encodes a functional SLC26A6 polypeptide encoded by the isolated nucleic acid of one of (a), (b), and (c) above.

30 29. The method of claim 26, wherein the host cell comprises a mammalian cell.

30. The method of claim 29, wherein the mammalian cell comprises a human cell.

31. The method of claim 26, wherein the SLC26A6 function comprises Cl⁻-formate exchange.
32. The method of claim 26, wherein the SLC26A6 function comprises Cl⁻-Cl⁻ exchange.
- 5 33. The method of claim 26, wherein the SLC26A6 function comprises SO₄²⁻ exchange.
34. The method of claim 26, wherein the SLC26A6 function comprises Cl⁻-oxalate exchange.
35. The method of claim 26, wherein the SLC26A6 function comprises Cl⁻-base exchange.
- 10 36. The method of claim 35, wherein the base comprises HCO₃⁻.
37. The method of claim 35, wherein the Cl⁻-base exchange comprises electrogenic transport.
38. An anion transporter modulator identified by the method of claim 26.
- 15 39. A method for modulating anion transport activity in a subject, the method comprising:
- (a) preparing a composition comprising a modulator identified according to the method of claim 26, and a pharmaceutically acceptable carrier;
 - 20 (b) administering an effective dose of the composition to a subject, whereby anion transport is altered in the subject.
40. The method of claim 39, wherein the subject is a mammal.
41. The method of claim 40, wherein the mammal is a human.
42. A method for identifying an anion exchanger modulator, the method
- 25 comprising:
- (a) exposing a SLC26A6 polypeptide to one or more test substances, wherein the SLC26A6 polypeptide comprises a mouse SLC26A6 polypeptide or a human SLC26A6a polypeptide;
 - 30 (b) assaying binding of a test substance to the isolated SLC26A6 polypeptide; and
 - (c) selecting a candidate substance that demonstrates specific binding to the SLC26A6 polypeptide.

43. The method of claim 42, wherein the mouse SLC26A6 polypeptide comprises:
- (a) a polypeptide of SEQ ID NO:6 or 8; or
 - (b) a polypeptide encoded by a nucleic acid molecule of SEQ ID NO:5 or 7.
44. The method of claim 42, wherein the mouse SLC26A6a polypeptide comprises:
- (a) a polypeptide of SEQ ID NO:2; or
 - (b) a polypeptide encoded by a nucleic acid molecule of SEQ ID NO:1.
45. An anion transporter modulator identified by the method of claim 42.
46. A method for modulating anion transport activity in a subject, the method comprising:
- (a) preparing a composition comprising a modulator identified according to the method of claim 42, and a pharmaceutically acceptable carrier;
 - (b) administering an effective dose of the composition to a subject, whereby SLC26 function is altered in the subject.
47. The method of claim 46, wherein the subject is a mammal.
48. The method of claim 47, wherein the subject is a human.
49. A method for modulating a SLC26A6 polypeptide in a subject, the method comprising administering an effective amount of a SLC26A6 modulator to the subject, wherein the SLC26A6 modulator comprises a pH modifier.
50. The method of claim 49, wherein the subject is a mammal.
51. The method of claim 50, wherein the mammal is a human.
52. An isolated nucleic acid encoding a mouse SLC26A1 polypeptide.
53. The isolated nucleic acid of claim 52, further comprising a nucleic acid encoding a polypeptide of SEQ ID NO:10.
54. The isolated nucleic acid of claim 52, further comprising a nucleic acid of SEQ ID NO:9.
55. An isolated mouse SLC26A1 polypeptide.

56. The isolated mouse SLC26A1 polypeptide of claim 55, further comprising:

- (a) a polypeptide encoded by a nucleic acid of SEQ ID NO:9; or
- (b) a polypeptide comprising an amino acid sequence of SEQ ID NO:10.

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57. The mouse SLC26A1 polypeptide of claim 55, further comprising a functional mouse SLC26A1 polypeptide.

58. A system for recombinant expression of a mouse SLC26A1 polypeptide, the system comprising:

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- (a) a mouse SLC26A1 polypeptide; and
- (b) a host cell comprising the mouse SLC26A1 polypeptide.

59. A method for identifying a modulator of a SLC26A1 polypeptide, the method comprising:

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- (a) providing a recombinant expression system whereby a functional mouse SLC26A1 polypeptide is expressed in a host cell;

- (b) providing a test substance to the system of (a);
- (c) assaying a level or quality of SLC26A1 function in the presence of the test substance;

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- (d) comparing the level or quality of SLC26A1 function in the presence of the test substance with a control level or quality of SLC26A1 function; and

- (e) identifying a test substance as an anion transport modulator by determining a level or quality of SLC26A1 function in the presence of the test substance as significantly changed when compared to a control level or quality of SLC26A1 function.

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60. The method of claim 57, wherein the mouse SLC26A1 comprises:

- (a) a polypeptide encoded by a nucleic acid of SEQ ID NO:9; or
- (b) a polypeptide comprising an amino acid sequence of SEQ ID NO:10.

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61. An anion transporter modulator identified by the method of claim 59.

62. A method for identifying an anion exchanger modulator, the method comprising:

- (a) exposing an isolated mouse SLC26A1 polypeptide to one or more test substances;
 - (b) assaying binding of a test substance to the isolated mouse SLC26A1 polypeptide; and
 - 5 (c) selecting a candidate substance that demonstrates specific binding to the SLC26A1 polypeptide.
63. The method of claim 62, wherein the mouse SLC26A1 comprises:
- (a) a polypeptide encoded by a nucleic acid of SEQ ID NO:9; or
 - (b) a polypeptide comprising an amino acid sequence of SEQ ID
10 NO:10.
64. An anion transporter modulator identified by the method of claim 62.
65. A method for activating a SLC26A1 polypeptide in a subject, the method comprising administering an effective amount of a SLC26A1 modulator to the subject, wherein the SLC26A1 modulator comprises an
15 impermeant anion.
66. The method of claim 65, wherein the impermeant anion comprises Cl⁻ or formate.
67. A method for modulating a SLC26A2 polypeptide in a subject, the method comprising administering an effective amount of a SLC26A2
20 modulator to the subject, wherein the SLC26A2 modulator comprises a pH modifier.
68. An isolated nucleic acid encoding a porcine SLC26A6 polypeptide.
69. The isolated nucleic acid of claim 68, further comprising a nucleic acid encoding a polypeptide of SEQ ID NO:91.
- 25 70. The isolated nucleic acid of claim 68, further comprising a nucleic acid of SEQ ID NO:90.
71. An isolated porcine SLC26A6 polypeptide.
72. The isolated porcine SLC26A6 polypeptide of claim 71, further comprising:
- 30 (a) a polypeptide encoded by a nucleic acid of SEQ ID NO:90; or
 - (b) a polypeptide comprising an amino acid sequence of SEQ ID NO:91.

73. An isolated nucleic acid encoding a *Xenopus laevis* SLC26A6 polypeptide.
74. The isolated nucleic acid of claim 73, further comprising a nucleic acid encoding a polypeptide of SEQ ID NO:89.
- 5 75. The isolated nucleic acid of claim 73, further comprising a nucleic acid of SEQ ID NO:88.
76. An isolated *Xenopus laevis* SLC26A6 polypeptide.
77. The isolated *Xenopus laevis* SLC26A6 polypeptide of claim 76, further comprising:
- 10 (a) a polypeptide encoded by a nucleic acid of SEQ ID NO:88; or
(b) a polypeptide comprising an amino acid sequence of SEQ ID NO:89.
78. An isolated nucleic acid encoding a *Xenopus laevis* SLC26A1 polypeptide.
- 15 79. The isolated nucleic acid of claim 78, further comprising a nucleic acid encoding a polypeptide of SEQ ID NO:87.
80. The isolated nucleic acid of claim 78, further comprising a nucleic acid of SEQ ID NO:86.
81. An isolated *Xenopus laevis* SLC26A1 polypeptide.
- 20 82. The isolated *Xenopus laevis* SLC26A1 polypeptide of claim 81, further comprising:
- (a) a polypeptide encoded by a nucleic acid of SEQ ID NO:86; or
(b) a polypeptide comprising an amino acid sequence of SEQ ID NO:87.
- 25 83. An isolated nucleic acid encoding a *Xenopus laevis* SLC26A4 polypeptide.
84. The isolated nucleic acid of claim 83, further comprising a nucleic acid encoding a polypeptide of one of SEQ ID NOs:81, 83, and 85.
85. The isolated nucleic acid of claim 83, further comprising a nucleic acid
30 of one of SEQ ID NOs:80, 82, and 84.
86. An isolated *Xenopus laevis* SLC26A4 polypeptide.
87. The isolated *Xenopus laevis* SLC26A4 polypeptide of claim 86, further comprising:

- (a) a polypeptide encoded by a nucleic acid of one of SEQ ID NOs:80, 82, and 84; or
- (b) a polypeptide comprising an amino acid sequence of one of SEQ ID NOs:81, 83, and 85.